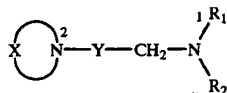


Appendix A

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What is claimed is:

1. A pharmaceutical composition for inhibiting cellular invasion or angiogenesis, wherein the composition comprises one or more cellular invasion or angiogenesis inhibiting compounds of formula I or II or pharmaceutically acceptable salts thereof, and a pharmaceutically acceptable carrier, wherein formula I is:



wherein:

X is a saturated, or unsaturated linear, branched, or partially cyclized alkyl chain of between eleven and thirty carbons optionally substituted with one or more substituents selected from the group consisting of: epoxide, ketone, thiocarbonyl, oxime, —OH, —OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, —COSR, —NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; wherein one or more CH₂ groups if present in the alkyl chain, is optionally replaced by a moiety selected from the group consisting of: O, S, NH and NR; and wherein one or more C and CH groups if present in the alkyl chain, is optionally replaced with NH or NR;

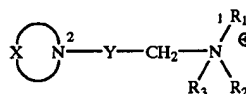
R₁ and R₂ are independently selected from the group consisting of: hydrogen; methyl; a linear, branched, or cyclic saturated, or unsaturated alkyl group containing one to ten carbons optionally substituted with one or more substituents selected from the group consisting of: —OH, —OR, —O, —S, —N—OH, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, —COSH, —COSR, —CSOR, NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; and benzyl, wherein a phenyl ring of the benzyl is optionally substituted with one or more substituents selected from the group consisting of: R, —OH, —OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NHR₂, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, —CONR₂, —COSH, —COSR, —NO₂, —SO₃H and —SO₂R; providing neither of R₁ and R₂ is an acyl or thioacyl residue forming an amide with N¹;

Y is a linear, branched, or cyclic, saturated, or unsaturated alkyl chain containing one to ten carbons optionally substituted with one or more substituents selected from the group consisting of: epoxide, —OH, —OR, —O, —S, —N—OH, —O₂CR, —SH, —SR, —I, —Br, —Cl, —F, —CN, —O₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, NO₂, —SOR and —SO₂R; wherein one or more CH₂ groups if present in the alkyl chain, is optionally replaced by O or S;

R is a linear, branched, or cyclic one to ten carbon saturated, or unsaturated alkyl group optionally substi-

tuted with one or more substituents selected from the group consisting of: epoxide, —OH, —OR, —O, —S, —N—OH, —O₂CR, —SH, —SR, —SOCR, —OSO₃H, —NH₂, —NHR, —NHR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, —CONR₂, —COSH, —COSR, —NO₂, —SO₃H, —SOR and —SO₂R; wherein R¹ is a linear, branched, or cyclic one to ten carbon, saturated or unsaturated alkyl group optionally substituted with —NH₂;

and wherein formula II is:



wherein: \odot colon

X is a saturated, or unsaturated linear, branched, or partially cyclized alkyl chain of between eleven and thirty carbons optionally substituted with one or more substituents selected from the group consisting of: epoxide, ketone, thiocarbonyl, oxime, —OH, —OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, —COSR, —NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; wherein one or more CH₂ groups in the alkyl chain if present, is optionally replaced by a moiety selected from the group consisting of: O, S, NH and NR; and wherein one or more C or CH groups in the alkyl chain if present, is optionally replaced with NH or NR;

R₁, R₂, and R₃ are independently selected from the group consisting of: methyl; a linear, branched, or cyclic, saturated, or unsaturated alkyl group containing one to ten carbons optionally substituted with one or more substituents selected from the group consisting of: —OH, —OR, —O, —S, —N—OH, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, —COSH, —COSR, —CSOR, NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; and benzyl, wherein a phenyl ring of the benzyl is optionally substituted with one or more substituents selected from the group consisting of: R, —OH, —OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NHR₂, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, —CONR₂, —COSH, —COSR, —NO₂, —SO₃H, —SOR and —SO₂R; providing none of R₁, R₂, and R₃ is an acyl or thioacyl residue forming an amide with N¹;

Y is a linear, branched, or cyclic, saturated, or unsaturated alkyl chain containing one to ten carbons optionally substituted with one or more substituents selected from the group consisting of: epoxide —OH, —OR, —O, —S, —N—OH, —O₂CR, —SH, —SR, —I, —Br, —Cl, —F, —CN, —CO₂R, —CHO, —COR,

dash

no dash

semi colon

—CONH₂, —CONHR, NRCOR, —CONR₂, NO₂, —SOR and —SO₂R; wherein one or more CH₂ groups if present in the alkyl chain, is optionally replaced by O or S; and,

R is a linear, branched, or cyclic one to ten carbon saturated, or unsaturated ^{alkyl} group optionally substituted with one or more substituents selected from the group consisting of: epoxide, —OH, —OR', —O, —S, —N—OH, —O₂CR', —SH, —SR', —SO₂CR', —OSO₂H, —NH₂, —NHR', —NHR'₂, —NR'₃⁺, —NHCOR', NR'₂COR', —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R', —CHO, —COR', —CONH₂, —CONHR', —CONR'₂, —COSH, —COSR', —NO₂, —SO₂H, —SOR' and —SO₂R', wherein R' is a linear, branched, or cyclic one to ten carbon, saturated, or unsaturated alkyl group optionally substituted with —NH₂.

2. The composition of claim 1, wherein Y is optionally substituted (CH₂)_n in which n is 1-5.

3. The composition of claim 1, wherein X is a saturated linear or branched alkyl chain of 11-16 carbon atoms, optionally substituted with R.

4. The composition of claim 1, wherein X is an unsaturated linear or branched alkyl chain of 11-16 carbon atoms, optionally substituted with R.

5. The composition of claim 1, wherein X is a fully unsaturated and partially cyclized linear alkyl chain of 11-16 carbon atoms, optionally substituted with R.

6. The composition of claim 1, wherein the compound is of formula I in which one or both R₁ and R₂ is a linear or branched alkyl group optionally substituted by a substituent selected from the group consisting of, NH₂, —NHR, —NR₂, —NR₃⁺ and —NHCOR.

7. The composition of claim 1, wherein the compound is of formula I in which one or both R₁ and R₂ is selected from the group consisting of: hydrogen; methyl; and a linear or branched alkyl group, optionally substituted with a substituent selected from the group consisting of: —OH, —OR, and —O.

8. The composition of claim 1, wherein the compound is of formula I in which one or both R₁ and R₂ is a linear or branched C₂ to C₆ alkyl group, optionally substituted with a substituent selected from the group consisting of: NH₂, —NHR, —NR₂, —NR₃⁺ and —NHCOR.

9. The composition of claim 1, wherein the compound is of formula I in which one or both R₁ and R₂ is selected from the group consisting of: hydrogen; methyl; and a linear or branched C₂ to C₆ alkyl group, optionally substituted with a substituent selected from the group consisting of: —OH, —OR, and —O.

10. The composition of claim 1, wherein the compound is of formula II in which one or more of R₁, R₂, and R₃ is a linear or branched alkyl group, optionally substituted with a substituent selected from the group consisting of: NH₂, —NHR, —NR₂, —NR₃⁺ and —NHCOR.

11. The composition of claim 1, wherein the compound is of formula II in which one or more of R₁, R₂, and R₃ is selected from the group consisting of: methyl; and a linear or branched alkyl group optionally substituted with a substituent selected from the group consisting of: —OH, —OR, and —O.

12. The composition of claim 1, wherein the compound is of formula II in which one or more of R₁, R₂, and R₃ is a linear or branched C₂ to C₆ alkyl group, optionally substituted with a substituent selected from the group consisting of: NH₂, —NHR, —NR₂, —NR₃⁺ and —NHCOR.

13. The composition of claim 1, wherein the compound is of formula II in which one or more of R₁, R₂, and R₃ is selected from the group consisting of: methyl; and a linear or branched C₂ to C₆ alkyl group, optionally substituted with a substituent selected from the group consisting of: —OH, —OR, and —O.

14. The composition of claim 1, wherein the compound is of formula I in which:

(a) Y is (CH₂)_n and n is 1, 2, or 3;

(b) X is a saturated or unsaturated linear alkyl chain of 11-15 carbon atoms, optionally substituted with a C₁-C₆ linear or branched alkyl group; or, a fully unsaturated and partially cyclized linear alkyl chain of 11-16 carbon atoms;

(c) one of R₁ and R₂ is selected from the group consisting of: H, methyl, and a linear or branched C₂-C₆ alkyl group; and,

(d) another of R₁ and R₂ is a linear or branched C₂-C₆ alkyl group optionally substituted with a substituent selected from the group consisting of: NH₂, —NHR, —NR₃⁺, and —NHCOR, wherein R is a linear or branched C₁-C₆ saturated or unsaturated alkyl group.

15. The composition of claim 1, wherein the compound is of formula II in which:

(a) Y is (CH₂)_n and n is 1, 2, or 3;

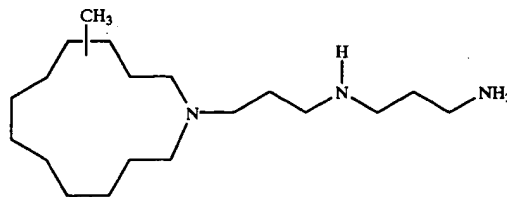
(b) X is a saturated or unsaturated linear alkyl chain of 11-15 carbon atoms, optionally substituted with, with a C₁-C₆ linear or branched alkyl group; or, a fully unsaturated and partially cyclized linear alkyl chain of 11-16 carbon atoms;

(c) one or two of R₁, R, and R₃ is methyl, or a linear or branched C₂-C₆ alkyl group; and,

(d) another of R₁, R, and R₃ is a linear or branched C₂-C₆ alkyl group optionally substituted with a substituent selected from the group consisting of: NH₂, —NHR, NR₃⁺ and —NHCOR, wherein R is a linear or branched C₁-C₆ saturated or unsaturated alkyl group.

16. The composition of claim 1, wherein the cellular invasion or angiogenesis inhibiting compound or compounds in the composition do not consist exclusively of Motuporamine A, B, or C, or mixtures thereof.

17. The composition of claim 1, wherein a compound in the composition has the structure:



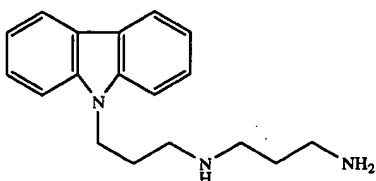
wherein the CH₃ group is joined at one of C-12, C-13, C-14 and C-15.

18. The composition of claim 1, wherein a compound in the composition is selected from the group consisting of: Motuporamine A, B, and C.

19. The composition of claim 1, wherein a compound in the composition is Motuporamine D.

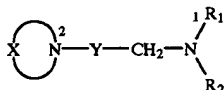
20. The composition of claim 1, wherein a compound in the composition is Dihydromotuporamine C.

21. The composition of claim 1, wherein a compound of the structure:



is present in the composition.

22. A cellular invasion or angiogenesis inhibiting compound of formula I or II in substantially purified form or a pharmaceutically acceptable salt thereof, where formula I is:



wherein:

X is a saturated, or unsaturated linear, branched, or partially cyclized alkyl chain of between eleven and thirty carbons optionally substituted with one or more substituents selected from the group consisting of: epoxide, ketone, thiocarbonyl, oxime, —OH, —OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, —COSR, —NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; wherein one or more CH₂ groups if present in the alkyl chain, is optionally replaced by a moiety selected from the group consisting of: O, S, NH and NR; and wherein one or more C and CH groups if present in the alkyl chain, is optionally replaced with NH or NR;

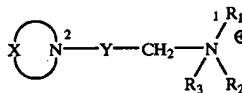
R₁ and R₂ are independently selected from the group consisting of: hydrogen; methyl; a linear, branched, or cyclic saturated, or unsaturated alkyl group containing one to ten carbons optionally substituted with one or more substituents selected from the group consisting of: —OH, —OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, —COSH, —COSR, —CSOR, —NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; and benzyl, wherein a phenyl ring of the benzyl is optionally substituted with one or more substituents selected from the group consisting of: R, —OH, —OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, —CONR₂, —COSH, —COSR, —CSOR, —NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; and

—COSR, —NO₂, —SO₃H and —SO₂R; providing neither of R₁ and R₂ is an acyl or thioacyl residue forming an amide with N¹;

Y is a linear, branched, or cyclic, saturated, or unsaturated alkyl chain containing one to ten carbons optionally substituted with one or more substituents selected from the group consisting of: epoxide, —OH, —OR, —O₂CR, —SH, —SR, —I, —Br, —Cl, —F, —CN, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, NO₂, —SOR and —SO₂R; wherein one or more CH₂ groups if present in the alkyl chain, is optionally replaced by O or S;

R is a linear, branched, or cyclic one to ten carbon saturated, or unsaturated alkyl group optionally substituted with one or more substituents selected from the group consisting of: epoxide, —OH, —OR', —O₂CR', —SH, —SR', —SOCR', —OSO₃H, —NH₂, —NHR', —NHR'₂, —NR₃⁺, —NHCOR', —NHCOR', —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R', —CHO, —COR', —CONH₂, —CONHR', —CONR'₂, —COSH, —COSR', —NO₂, —SO₃H, —SOR' and —SO₂R', wherein R' is a linear, branched, or cyclic one to ten carbon, saturated, or unsaturated alkyl group optionally substituted with —NH₂;

and wherein formula II is:



wherein:

X is a saturated, or unsaturated linear, branched, or partially cyclized alkyl chain of between eleven and thirty carbons optionally substituted with one or more substituents selected from the group consisting of: epoxide, ketone, thiocarbonyl, oxime, —OH, —OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, —COSR, —NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; wherein one or more CH₂ groups in the alkyl chain if present, is optionally replaced by a moiety selected from the group consisting of: O, S, NH and NR; and wherein one or more C or CH groups in the alkyl chain if present, is optionally replaced with NH or NR;

R₁, R₂, and R₃ are independently selected from the group consisting of: methyl; a linear, branched, or cyclic, saturated, or unsaturated alkyl group containing one to ten carbons optionally substituted with one or more substituents selected from the group consisting of: —OH, —OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, —COSH, —COSR, —CSOR, —NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; and

benzyl, wherein a phenyl ring of the benzyl is optionally substituted with one or more substituents selected from the group consisting of: R, —OH, OR, —O₂CR, —SH, —SR, —SO₂CR, —NH₂, —NHR, —NHR₂, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, —CONR₂, —COSH, —COSR, —NO₂, SO₃H, —SOR and —SO₂R; providing none of R₁, R₂, and R₃ is an acyl or thioacyl residue forming an amide with N⁺;

Y is a linear, branched, or cyclic, saturated, or unsaturated alkyl chain containing one to ten carbons optionally substituted with one or more substituents selected from the group consisting of: epoxide —OH, —OR, =O, =S, =N—OH, —O₂CR, —SH, —SR, —I, —Br, —Cl, —F, —CN, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, NO₂, —SOR and —SO₂R; wherein one or more CH₂ groups if present in the alkyl chain, is optionally replaced by O or S; and,

R is a linear, branched, or cyclic one to ten carbon saturated, or unsaturated alkyl group optionally substituted with one or more substituents selected from the group consisting of: epoxide, —OH, —OR', =O, =S, =N—OH, —O₂CR', —SH, —SR', —SO₂CR', —OSO₃H, —NH₂, —NHR', —NHR'₂, —NR'₃+, —NHCOR', NR'COR', —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R', —CHO, —COR', —CONH₂, —CONHR', —CONR'₂, —COSH, —COSR', —NO₂, —SO₃H, —SOR' and —SO₂R' wherein R' is a linear, branched, or cyclic one to ten carbon, saturated, or unsaturated alkyl group optionally substituted with —NH₂;

and providing that the compound is not Motuporamine A, B, or C.

23. The compound of claim 22, wherein Y is optionally substituted (CH₂)_n in which n is 1-5.

24. The compound of claim 22, wherein X is a saturated linear or branched alkyl chain of 11-16 carbon atoms, optionally substituted with R.

25. The compound of claim 22, wherein X is an unsaturated linear or branched alkyl chain of 11-16 carbon atoms, optionally substituted with R.

26. The compound of claim 22, wherein X is a fully unsaturated and partially cyclized linear alkyl chain of 11-16 carbon atoms, optionally substituted with R.

27. The compound of claim 22, wherein the compound is of formula I in which one or both R₁ and R₂ is a linear or branched alkyl group optionally substituted by a substituent selected from the group consisting of: NH₂, —NHR, —NR₂, —NR₃+, and —NHCOR.

28. The compound of claim 22, wherein the compound is of formula I in which one or both R₁ and R₂ is selected from the group consisting of: hydrogen; methyl; and a linear or branched alkyl group, optionally substituted with a substituent selected from the group consisting of: —OH, —OR, and =O.

29. The compound of claim 22, wherein the compound is of formula I in which one or both R₁ and R₂ is a linear or branched C₂ to C₆ alkyl group, optionally substituted with a substituent selected from the group consisting of: NH₂, —NHR, —NR₂, —NR₃+, and —NHCOR.

30. The compound of claim 22, wherein the compound is of formula I in which one or both R₁ and R₂ is selected from the group consisting of: hydrogen; methyl; ~~and~~ a linear or branched C₃ to C₆ alkyl group, optionally substituted with a substituent selected from the group consisting of: —OH, —OR, and =O.

31. The compound of claim 22, wherein the compound is of formula II in which one or more of R₁, R₂, and R₃ is a linear or branched alkyl group, optionally substituted with a substituent selected from the group consisting of: NH₂, —NHR, —NR₂, —NR₃+, and —NHCOR.

32. The compound of claim 22, wherein the compound is of Formula II in which one or more of R₁, R₂, and R₃ is selected from the group consisting of: methyl; and a linear or branched alkyl group optionally substituted with a substituent selected from the group consisting of: —OH, —OR, and =O.

33. The compound of claim 22, wherein the compound is of formula II in which one or more of R₁, R₂, and R₃ is a linear or branched C₂ to C₆ alkyl group, optionally substituted with a substituent selected from the group consisting of: NH₂, —NHR, —NR₂, —NR₃+, and —NHCOR.

34. The compound of claim 22, wherein the compound is of formula II in which one or more of R₁, R₂, and R₃ is selected from the group consisting of: methyl; and a linear or branched C₂ to C₆ alkyl group, optionally substituted with a substituent selected from the group consisting of: —OH, —OR, and =O.

35. The compound of claim 22, wherein the compound is of formula I in which:

(a) Y is (CH₂)_n and n is 1, 2, or 3;

(b) X is a saturated or unsaturated linear alkyl chain of 11-15 carbon atoms, optionally substituted with a C₁-C₆ linear or branched alkyl group; or, a fully unsaturated and partially cyclized linear alkyl chain of 11-16 carbon atoms;

(c) one of R₁ and R₂ is selected from the group consisting of: H, methyl, and a linear or branched C₂-C₆ alkyl group; and,

(d) another of R₁ and R₂ is a linear or branched C₂-C₆ alkyl group optionally substituted with a substituent selected from the group consisting of: NH₂, —NHR, —NR₃+, and —NHCOR, wherein R is a linear or branched C₁-C₆ saturated or unsaturated alkyl group.

36. The compound of claim 22, wherein the compound is of formula II in which:

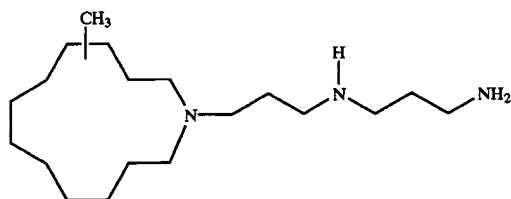
(a) Y is (CH₂)_n and n is 1, 2, or 3;

(b) X is a saturated or unsaturated linear alkyl chain of 11-15 carbon atoms, optionally substituted with R, with a C₁-C₆ linear or branched alkyl group; or, a fully unsaturated and partially cyclized linear alkyl chain of 11-16 carbon atoms;

(c) one or two of R₁, R, and R₃ is methyl, or a linear or branched C₂-C₆ alkyl group; and,

(d) another of R₁, R, and R₃ is a linear or branched C₂-C₆ alkyl group optionally substituted with a substituent selected from the group consisting of: NH₂, —NHR, NR₃+, and —NHCOR, wherein R is a linear or branched C₁-C₆ saturated or unsaturated alkyl group.

37. The compound of claim 22, wherein the compound has the structure:

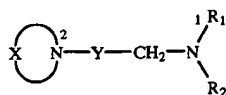


wherein the CH₃ group is joined at one of C12, C-13, C-14 and C-15.

38. The compound of claim 22, wherein the compound is Motuporamine D.

39. The compound of claim 22, wherein the compound is Dihydromotuporamine C.

40. A method for inhibiting cellular invasion or angiogenesis in a patient in need thereof, comprising administering to the patient, an amount of a compound or pharmaceutically acceptable salt thereof effective to inhibit cellular invasion or angiogenesis in a tissue of the patient, the compound being of formula I or II, wherein formula I is:



wherein:

X is a saturated, or unsaturated linear, branched, or partially cyclized alkyl chain of between eleven and thirty carbons optionally substituted with one or more substituents selected from the group consisting of: epoxide, ketone, thiocarbonyl, oxime, —OH, —OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, —COSR, —NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; wherein one or more CH₂ groups if present in the alkyl chain, is optionally replaced by a moiety selected from the group consisting of: O, S, NH and NR; and wherein one or more C and CH groups if present in the alkyl chain, is optionally replaced with NH or NR;

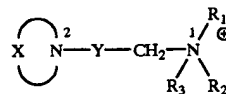
R₁ and R₂ are independently selected from the group consisting of: hydrogen; methyl; a linear, branched, or cyclic saturated, or unsaturated alkyl group containing one to ten carbons optionally substituted with one or more substituents selected from the group consisting of: —OH, —OR, —O, —S, —N—OH, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, —COSH, —COSR, —CSOR, NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; and benzyl, wherein a phenyl ring of the benzyl is optionally substituted with one or more substituents selected from the group consisting of: R,

—OH, —OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NHR₂, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, —CONR₂, —COSH, —COSR, —NO₂, —SO₃H and —SO₂R; providing neither of R₁ and R₂ is an acyl or thioacyl residue forming an amide with N¹;

Y is a linear, branched, or cyclic, saturated, or unsaturated alkyl chain containing one to ten carbons optionally substituted with one or more substituents selected from the group consisting of: epoxide, —OH, —OR, —O, —S, —N—OH, —O₂CR, —SH, SR, —I, —Br, —Cl, —F, —CN, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, NO₂, —SOR and —SO₂R; wherein one or more CH₂ groups if present in the alkyl chain, is optionally replaced by O or S;

R is a linear, branched, or cyclic one to ten carbon saturated, or unsaturated alkyl group optionally substituted with one or more substituents selected from the group consisting of: epoxide, —OH, —OR', —O, —S, —N—OH, —O₂CR', —SH, —SR', —SOCR', —OSO₃H, —NH₂, —NHR', —NHR'₂, —NR'₃⁺, —NHCOR', NR'COR', —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R', —CHO, —COR', —CONH₂, —CONHR', —CONR'₂, —COSH, —COSR', —NO₂, —SO₃H, —SOR' and —SO₂R'; wherein R' is a linear, branched, or cyclic one to ten carbon, saturated, or unsaturated alkyl group optionally substituted with —NH₂;

and wherein formula II is:



wherein:

X is a saturated, or unsaturated linear, branched, or partially cyclized alkyl chain of between eleven and thirty carbons optionally substituted with one or more substituents selected from the group consisting of: epoxide, ketone, thiocarbonyl, oxide, —OH, —OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, NRCOR, —CONR₂, —COSR, —NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; wherein one or more CH₂ groups in the alkyl chain if present, is optionally replaced by a moiety selected from the group consisting of O S, NH and NR; and wherein one or more C or CH groups in the alkyl chain if present, is optionally replaced with NH or NR;

R₁, R₂, and R₃ are independently selected from the group consisting of: methyl; a linear, branched, or cyclic, saturated, or unsaturated alkyl group containing one to ten carbons optionally substituted with one or more substituents selected from the group consisting of: —OH, —OR, —O, —S, —N—OH, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NR₂, —NR₃⁺, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂R, —CHO, —COR, —CONH₂, —CONHR,

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NRCOR, —CONR₂, —COSH, —COSR, —CSOR, NO₂, —OSO₃H, —SO₃H, —SOR and —SO₂R; and benzyl, wherein a phenyl ring of the benzyl is optionally substituted with one or more substituents selected from the group consisting of: R, —OH, OR, —O₂CR, —SH, —SR, —SOCR, —NH₂, —NHR, —NHR₂, —NHCOR, —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, —CONR₂, —COSH, —COSR, —NO₂, SO₃H, —SOR and —SO₂R; providing none of R₁, R₂, and R₃ is an acyl or thioacyl residue forming an amide with N¹;

Y is a linear, branched, or cyclic, saturated, or unsaturated alkyl chain containing one to ten carbons optionally substituted with one or more substituents selected from the group consisting of: epoxide —OH, —OR, =O, =S, =N—OH, —O₂CR, —SH, —SR, —I, —Br, —Cl, —F, —CN, —CO₂R, —CHO, —COR, —CONH₂, —CONHR, —CONR₂, NRCOR, —CONR₂, NO₂, —SOR and —SO₂R; wherein one or more CH₂ groups if present in the alkyl chain, is optionally replaced by O or S; and,

R is a linear, branched, or cyclic one to ten carbon saturated, or unsaturated alkyl group optionally substituted with one or more substituents selected from the group consisting of: epoxide, —OH, —OR', =O, =S, =N—OH, —O₂CR', —SH, —SR', —SOCR', —OSO₃H, —NH₂, —NHR', —NHR'₂, —NR'₃+, —NHCOR', NR'COR', —I, —Br, —Cl, —F, —CN, —CO₂H, —CO₂R', —CHO, —COR', —CONH₂, —CONHR', —CONR'₂, —COSH, —COSR', —NO₂, —SO₃H, —SOR' and —SO₂R'; wherein R' is a linear, branched, or cyclic one to ten carbon, saturated, or unsaturated alkyl group optionally substituted with —NH₂.

41. The method of claim 40, wherein

(a) Y is (CH₂)_n and n is 1, 2, or 3;

(b) X is a saturated or unsaturated linear chain of 11-15 carbon atoms, optionally substituted with a C₁-C₆ linear or branched alkyl group; or, a fully unsaturated and partially cyclized linear alkyl chain of 11-16 carbon atoms;

(c) one of R₁ and R₂ is selected from the group consisting of: H, methyl, and a linear or branched C₂-C₆ alkyl group; and,

(d) another of R₁ and R₂ is a linear or branched C₂-C₆ alkyl group optionally substituted with a substituent selected from the group consisting of: NH₂, —NHR, —NR₃+, and —NHCOR, wherein R is a linear or branched C₁-C₆ saturated or unsaturated alkyl group.

42. The method of claim 40, wherein the compound is of formula II in which:

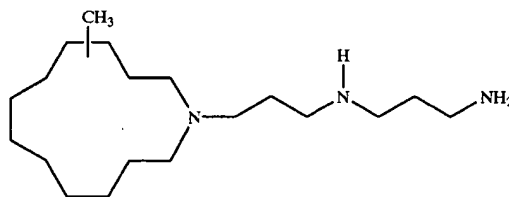
(a) Y is (CH₂)_n and n is 1, 2, or 3;

(b) X is a saturated or unsaturated linear alkyl chain of 11-15 carbon atoms, optionally substituted with R, with a C₁-C₆ linear or branched alkyl group; or, a fully unsaturated and partially cyclized linear alkyl chain of 11-16 carbon atoms;

(c) one or two of R₁, R, and R₃ is methyl, or a linear or branched C₂-C₆ alkyl group; and

(d) another of R₁, R, and R₃ is a linear or branched C₂-C₆ alkyl group optionally substituted with a substituent selected from the group consisting of: NH₂, —NHR, —NR₃+, and —NHCOR, wherein R is a linear or branched C₁-C₆ saturated or unsaturated alkyl group.

43. The method of claim 40, wherein a compound in the composition has the structure:



wherein the CH₃ group is joined at one of C12, C-13, C-14 and C-15.

44. The method of claim 40, wherein the compound is selected from the group consisting of Motuporamine A, B, and C.

45. The method of claim 40, wherein the compound is Motuporamine D.

46. The method of claim 40, wherein the compound is Dihydromotuporamine C.

47. A method for testing for the presence of an agent that inhibits cellular invasion comprising:

(a) placing cells on a surface of a biological matrix into which said cells are capable of invasion;

(b) treating said cells with an agent to be tested for cellular invasion inhibition activity;

(c) maintaining the cells on the surface of the matrix for a time sufficient for the cells to invade the matrix in the absence of an agent which inhibits cellular invasion;

(d) removing substantially all cells from the surface of the matrix after (c);

(e) transferring the cells removed at (d) to a surface upon which said cells are capable of attachment and proliferation;

(f) maintaining the cells on a surface at (e) for a time sufficient for cellular attachment and proliferation on the surface;

(g) determining a value indicative of a quantity of cells attached to said surface after (f); and,

(h) comparing the value determined at (g) to a control value determined by performing (a), (c), (d), (e), (f) and (g) with the cells in the absence of an agent that inhibits cellular invasion.

48. The method of claim 47, wherein the cells are cancer cells.

49. The method of claim 47, wherein the matrix is a membrane or a gel.

50. The method of claim 49, wherein the matrix comprises Matrigel™.

* * * * *